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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,338	12/07/2001	Patrice Denefle	03806.0529	9446

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EXAMINER	
NGUYEN, DAVE TRONG	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,338	DENEFLE ET AL.	
	Examiner	Art Unit	
	Dave T Nguyen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-45* is/are pending in the application.

4a) Of the above claim(s) *7-20,25-33,36-43 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,21-24,34,35 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claim 2 has been canceled, claims 1, 3-6 have been amended by the amendment filed August 24, 2004.

Claim 45 has been added by the amendment dated December 2, 2003.

Claims 7-20, 25-33, 36-43, and 45, drawn to non-elected claimed invention, remain withdrawn from further consideration by the Examiner, 37 C.F.R. 1.142(b), as being drawn to a non-elected invention.

Elected Claims 1, 3-6, 21-24, 34, 35 and 44 are pending for examination.

35 U.S.C. 101

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The claimed invention (claims 1, 3-6, 21-24, 35, 35, and 44) as elected lacks patentable utility. The as-filed application discloses that SEQ ID NOS: 1-4 are homologous to one another and are sequenced from a cluster of genes present in Chromosome 17q24, encode amino acid sequences which are 43% - 62% identical among another, and encodes a C-terminal amino acid sequence which is claimed as a C-terminal ATP binding domain. The application further discloses on page 10 bridging page 11:

(028) The present invention relates to nucleic acids corresponding to the

various human ABCAS, ABCA6, ABCA9, and ABCAIO genes, which are likely to be involved in the reverse transport of cholesterol, as well as in the membrane transport of lipophilic molecules, in particular, inflammation-mediating substances such as prostaglandins and prostacyclins, or in any pathology whose candidate chromosomal region is situated on chromosome 17, more precisely on the 17q arm and, still more precisely, in the 17q24 locus.

The application further discloses on page 10:

(026) Furthermore, each of the newly discovered genes is transcribed with a tissue-specific distribution and presents a heterogenous pattern of expression, suggesting a regional and probably functional specialization of the corresponding proteins.

On the basis of the above information, applicant formulate claims readable on SEQ ID NO: 1, and a genus of genes which hybridizes to SEQ ID NO: 1, or which has at least 80% sequence identity to SEQ ID NO: 1.

It is clear from the instant specification that the " ABCA5" gene described as SEQ ID NO: 1 or SEQ ID NO: 5 are claimed as being similar to other known ABCA genes such as the ABCA1 gene, wherein the members are not necessarily related in its substantial utility and essential structure for its corresponding biological function. In fact, the as-filed specification provides written description to support this notion, see page 10, par. 26 (cited above). Moreover, the as-filed specification states on page 3:

(005) Analysis of amino acids sequence alignments of the ATP-binding domains has allowed the ABC genes to be separated into sub-families (Allikmets et al., Hum Mol Genet, 1996, 5, 1649-1655). Currently, according to the recent HUGO classification, seven ABC gene sub-families named ABC (A to G) have been described in the human genome (ABCI, CFTR/MRP, MDR, ABC8, ALD, GCN20, OABP) with all except one (OABP) containing multiple members. For the most part, these sub-families contain genes that also display considerable conservation in the transmembrane domain sequences and have similar gene organization. However, ABC proteins transport very varied substrates, and some members of different sub-families have been shown to share more similarity in substrate recognition than do proteins within the same sub-family. Five of the sub-families also are represented in the yeast genome, indicating that these groups have been retained from an early time in the evolution of eukaryotes (Decottignies et al., Naf Genef, 1997, 137-45', Michaelis et al., 1995, Cold Spring Harbor Laboratory Press).

The as-filed specification further acknowledges on page 5 that a simple showing of a tissue specific expression of other genes claimed to be ABCA2 and ABCA3 does not necessarily mean that its respective function can be ascribed to the ABCA2 or ABCA3 genes.

Other than the general information provided by the as-filed specification as indicated above, the as-filed specification does not provide any written description of

what is exactly the function of the claimed ABCA5 gene. There is little doubt that, after complete characterization, this DNA and protein, may be found to have a specific and substantial utility in the transport of cholesterol, for example, wherein this described function would lead a skilled artisan to envision a substantial and specific utility for the claimed gene. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete, and thus, lacks a substantial utility for the claimed invention at the time the invention was made. The instant situation is directly analogous to that which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were know to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts where this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101 which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. Note that a utility that requires or constitutes carrying out further research or identify or reasonably confirm a real world context of use is not a substantial utility.

The as-filed specification does not provide any information or written support to show a substantial utility for the subject matter being sought in the presently pending claims, particularly since it is well-recognized in the art and in the as-field specification that ABC genes belong to a superfamilty of genes whose members have been

demonstrated a broad range of specific and biological activities involving in transporting distinct molecules such as organic and inorganic ions, peptides, and proteins, heavy metals, steroids, lipids, cholesterol, see Table 2 of Efferth, Current Molecular Medicine, Vol. 1, 45-65, 2001. The number of ATP-binding cassette (ABC) transporter genes isolated so far is enormous, wherein the members are functionally diverse, and thus, a disclosure of a nucleotide sequence or gene which is found to be homologous to a known ABCA gene such as the ABCA1 gene does not necessarily mean a substantial utility can be reasonably assessed by a skilled artisan, particularly on the basis of the as-filed specification. Also see Dean, Genomic Research, Vol. 11, pp. 1156-66. 2001, particularly abstract, Table 1; Thomas Efferth, Ageing Res. Reviews, 2, 11-24, 2003, abstract; and Annilo, Mammalian Genome, 14, 1, 7-20, 2003, page 7 bridging page 8. The doubts expressed in the prior art with respect to the lack of correlation between sequence homology and tissue specific distribution of a ABCA gene and its function, without a further investigation of its specific function, is further substantiated in Petry, Biochemical and Biophysical Res Comm., 300, 343-350, 2003, see the abstract, for example.

As such, one skilled in the art could not predict which biological activity is possessed by the claimed ABCA1 gene based on structural similarity, its tissue specific distribution, or even its location on the chromosome 17q24, particularly there is substantial evidence provided both in the as-filed specification and the art of record that ABC member share structural similarity, but not necessarily functional similarity. Neither the as-filed specification nor the prior art of record at the time the invention was made

provides any factual evidence to indicate that as the as-filed specification provides a substantial utility for the subject matter being sought in the presently pending claims.

The specification as a whole clearly generalizes and merely discloses, for example, that the ABCA5 gene is likely "to be involved in the reverse transport of cholesterol, as well as in the membrane transport of lipophilic molecules, in particular, inflammation-mediating substances such asprostaglandins and prostacyclins, or in any pathology whose candidate chromosomal region is situated on chromosome 17, more precisely on the 17q arm and, still more precisely, in the 17q24 locus. These possible utilities-other than as a possible object of scientific inquiry-was not yet established by the as-filed specification at the time the invention was made.

In view of the reasons set forth above, a skilled artisan would not have recognized that, at the time the invention was made, this as-filed specification provides any credible support for a substantial utility for the subject matter being sought in the presently pending claims.

Applicant's response (pages 8-9) has been considered fully by the examiner, but is not found persuasive for the reasons as set forth in the rejection.

More specifically, applicant's cites a number of paragraphs from the as-filed specification, which appears to indicates a number of diseases that ABC5 may be involved, and may be used as a DNA or protein drug. However, such paragraphs do not negate the evidential support and particular reasoning as set forth in the sated rejection, which do show that one skilled in the art could not predict which biological activity is

possessed by the claimed ABCA1 gene based on structural similarity, its tissue specific distribution, or even its location on the chromosome 17q24, particularly there is substantial evidence provided both in the as-filed specification and the art of record that ABC member share structural similarity, but not necessarily functional similarity. Neither the as-filed specification nor the prior art of record at the time the invention was made provides any factual evidence to indicate that as the as-filed specification provides a substantial utility for the subject matter being sought in the presently pending claims.

The specification as a whole clearly generalizes and merely discloses, for example, that the ABCA5 gene is likely "to be involved in the reverse transport of cholesterol, as well as in the membrane transport of lipophilic molecules, in particular, inflammation-mediating substances such asprostaglandins and prostacyclins, or in any pathology whose candidate chromosomal region is situated on chromosome 17, more precisely on the 17q arm and, still more precisely, in the 17q24 locus. These possible utilities-other than as a possible object of scientific inquiry-was not yet established by the as-filed specification at the time the invention was made.

In view of the reasons set forth above, a skilled artisan would not have recognized that, at the time the invention was made, this as-filed specification provides any credible support for a substantial and specific utility for the subject matter being sought in the presently pending claims.

The phrase "an isolated nucleic acid comprising any one of SEQ ID NO: 1, or of a complementary sequence," can be reasonably interpreted broadly as any isolated

nucleic acid sequence comprising any fragment of SEQ ID NO: 1, or of any nucleotide sequence which is partially complementary to SEQ ID NO:1, particularly when read in light of the as-filed specification. Thus, the following ground of the rejection would reflect the claim interpretation.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Elected claims 1, 3-6, 21-24, 34, 35 and 44, embracing claimed subject matter of variants of ABCA5 genes, and/or genes that are not necessarily the ABCA5 gene, but rater code for any gene that happens to share at least 80% nucleotide identity, or to hybridize under high stringency conditions with a nucleic acid comprising any nucleotide sequence of SEQ ID NO: 1, which are yet to be discovered, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The as-filed specification only provides sufficient written description of the ABCA5 gene, which is SEQ ID NO: 1. Even with claims that may embrace sequences and/or genes that are at least 80% identical to SEQ ID NO: 1, wherein the sequences and/or genes are involved in the reverse transport of cholesterol, as well as in the membrane transport lipophilic molecules, or in any pathology whose candidate chromosomal region is situated on chromosome 17, the as-filed specification does not provide sufficient description for such claimed subgenus.

An adequate written description of a polypeptide or protein or peptide requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the core structure of the claimed protein or polypeptide sequences itself. It is not sufficient to have description of SEQ ID NO: 1, and/or to define the claimed genus of nucleic acid sequences on the basis of a generic principal biological property, i.e. likely to be involved in the reverse transport of cholesterol, as well as in the membrane transport lipophilic molecules, or in any pathology whose candidate chromosomal region is situated on chromosome 17, and/or to define the claimed CCR protein sequences solely by percentage identify or hybridization, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of a genus of other genes that are yet to be discovered or characterized. Even with the subgenus of ABC coding DNA as claimed, the family of proteins capable of acting as ABC proteins is diverse and enormous, and that any ABC is capable of binding to a ATP. The claims as written clearly embrace a genus of ABC proteins, let alone other unrelated genes, which have nothing to do with SEQ ID NO: 1,

and thus, the as-filed specification does not reasonably provide sufficient description of a representative number of ABC polypeptide sequences comprising a particular primary structure amino acid residues, which are embraced by the breadth of the claimed invention. Claiming a genus of unspecified gene sequences coding for a ABC that are yet to be discovered, wherein the essential feature of the particular sequences of a ABC protein that would distinguish said ABC protein from other ABC proteins in the ABC gene family, that achieve a result without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

Applicant's response on page 9 has been considered by the examiner fully but also is not found persuasive. Applicant asserts that in view of the fragments obtained from SEQ ID NO: 1 and a number of potential permutations with respect to a conservative amino acid substitution, *e.g.,* hydrophobic amino acid to another hydrophobic amino acid, a polar amino acid to another polar amino acid, applicant meets the written description requirement. The assertion is not persuasive because the claims are not limited to fragments of SEQ ID NO: 1. Furthermore, the as-filed application does not at all provide a specific description of the entire sequence structure such permutated sequences, let alone the full sequence structure of a representative number of species of sequences as embraced by the broadly claimed genus of DNA or nucleic acid sequences. Note also that a search and review of the prior art of record does not provide any evidentiary support showing that without a further research, a

skilled artisan could readily envision the sequence structure of a variant of ABC5 on the basis of just potential additions, deletions, and substitutions that may be applied randomly to amino acid residues as set forth in SEQ ID NO: 1. Note also that the claims also embrace isolated naturally occurring variants of SEQ ID NO: 1 and/or unrelated genes, which are clearly yet to be discovered by the as-filed specification.

Claims 1, 3-6, 21-24, 34, 35 and 44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In view of the reasons set forth in the preceding paragraphs, a skilled artisan, without any undue experimentation, would not be able to make and /or use the invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 21-24, 34, 35 and 44 are rejected under 35 USC 102(e) as being anticipated by Hu (WO 02/31147 A2, which relies upon US provisional application 60/239,629 for priority, which application is also attached to this office action).

While the claim amendment obviates one of the claimed embodiments, which are drawn to an isolated nucleic acid sequence which is 80.4% identical to the entire sequence as set forth in SEQ ID NO: 1, such does not obviate the rejection over another embodiment, which is drawn to an isolated nucleic acid sequence, which is 99.8% identical to nucleotide residues 757-6014 of SEQ ID NO: 1. Another embodiment is drawn to an isolated nucleic acid comprising nucleotide residues 757-2316 of SEQ ID NO: 1. The claims also embrace an isolated nucleic acid that hybridizes under high stringency conditions with SEQ ID NO: 1 and any nucleotide sequence of SEQ ID NO: 1.

These claimed embodiments are anticipated by Hu because Hu teaches SEQ ID NO: 5 (which is also identified as SEQ ID NO: 5 in the '629 application), which not only is 99.8% identical to nucleotide residues 757-6014 of SEQ ID NO: 1, but also comprises nucleotide residues 757-2316 of SEQ ID NO: 1. Vectors and recombinant host cells, which comprise the sequence, are disclosed on pages 3, 10, and 11 of the '629 application. Sequences that hybridizes under highly stringent conditions with the sequence is also disclosed on page 4 of the '629 application. Complementary sequences are also disclosed on the last par. of page 4. Pharmaceutical composition comprising a bioreactor having the recombinant host cells is also disclosed on pages 12, 18, 19, and 24 of the '629 application.

Thus, the claims are anticipated by the Hu reference.

Applicant's response on page 9 is not found persuasive for obviating the prior art rejection of record, particularly in view of the reasons as set forth in the stated rejection.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **571-272-0731**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Amy Nelson*, may be reached at **571-272-0184.**

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center number, which is **703-872-9306.**

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Nguyen
Primary Examiner
Art Unit: 1632

DAVE T. NGUYEN
PRIMARY EXAMINER